Discussion

The one-electron reduction [by e_{aq}^- or by electron transfer from the $(CH_3)_2\dot{C}OH$ radical] of nicotinamide leads, in neutral solution, to the reduction and *rapid* protonation of the ring nitrogen. The odd electron is in conjugation with the ring and the 3-$CONH_2$ group. Esr results[25] on the reduction of pyridine compounds are in agreement with this assignment. The reduction of N_1-methylnicotinamide and NAD^+ also probably takes place initially at the ring nitrogen. Ionization of the $-\dot{N}H-$ radical has been observed for the first time and occurs at very high pH values (see Table II). This high pK_a (radical) value for nicotinamide is consistent with the correlation[26] between the ionization constants of free radicals and the redox potentials of the parent compounds.

Another novel feature is the suggested protonation on oxygen in very acidic solutions; see Schemes I–IV. It is interesting to note that in acid solutions the one-electron reduction of benzoylpyridines[27] was suggested to form a radical with protonation of both the ring nitrogen and the carbonyl group. However, the first proton to ionize was suggested[27] to be the $-\dot{N}H-$ proton followed, in alkaline solutions, by the $-\dot{C}(OH)-$ proton. In view of the results obtained above with different nicotinamides, the assignment for the benzoylpyridines may be incorrect and should be reversed [*i.e.*, the first proton to ionize may be coming from the $-C(OH)-$ group].

The $\cdot NH$ and $\cdot MN$ radicals present in neutral solutions are relatively strong reducing agents and have kinetic redox potentials of ~ -0.90 V; see Table III. The $NAD\cdot$ radical with a $E^{01} = -0.75$ V is a weaker reducing agent. However, the three radicals can react with oxygen to regenerate the parent compound[16,28] (possibly *via* a peroxy radical as an intermediate)

$$\cdot NH + O_2 \longrightarrow N + \cdot O_2^- + H^+$$

(25) H. Zeldes and R. Livingston, *J. Phys. Chem.*, 77, 2076 (1973); P. Neta and R. W. Fessenden, *Chem. Phys. Lett.*, 18, 14 (1973).

(26) P. S. Rao and E. Hayon, *J. Phys. Chem.*, to be submitted for publication.

(27) D. A. Nelson and E. Hayon, *J. Phys. Chem.*, 76, 3200 (1972).

(28) A. J. Swallow, *Isr. J. Chem.*, 10, 999 (1972).

This reaction is consistent with the determined[29,30] redox potential for the $O_2/\cdot O_2^-$ redox couple.

Electron transfer from $\cdot NH$, $\cdot MN$, $\cdot i$-NH, and $NAD\cdot$ radicals to a range of electron-acceptor compounds can be observed to take place; see Table IV.

Table IV. Reaction Rate Constants for Electron Transfer from Some Nicotinamide Free Radicals to Selected Acceptors in Aqueous Solution (at pH 7.0)

Donor radical	Acceptor compd[a] (V)	k, M^{-1} sec^{-1} [b]
Nicotinamide ($\cdot NH$)	Eosin Y (-0.50)	2.5×10^9
	Menaquinone ($+0.002$)	5.1×10^9
	p-Benzoquinone ($+0.293$)	5.0×10^9
Nicotinic acid ($\cdot NAH$)	Eosin Y (-0.50)	3.0×10^9
	Menaquinone ($+0.002$)	4.4×10^9
	p-Benzoquinone ($+0.293$)	5.2×10^9
N-Methylnicotinamide ($\cdot MN$)	3-Benzoylpyridine (-0.75)	2.6×10^9
	Menaquinone ($+0.002$)	4.9×10^9
	p-Benzoquinone ($+0.293$)	5.2×10^9
NAD^+ ($NAD\cdot$)	Riboflavin (-0.208)	1.0×10^9
	Oxygen	2.0×10^9
	Menaquinone ($+0.002$)	3.1×10^9
	p-Benzoquinone ($+0.293$)	4.4×10^9, 3.6×10^9

[a] Values in parentheses are the redox potentials E^{01} of the acceptors at pH 7.0. [b] From ref 16.

These rate constants reach near diffusion-controlled rates of $\leq 6.0 \times 10^9$ M^{-1} sec^{-1}. All these electron acceptors have redox potentials which are more positive than the kinetic potentials of the donor radials.

Thus, nicotinamide, nicotinic acid, and isonicotinamide are not as readily reduced by one-electron reducing agents, compared to N_1-methylnicotinamide and NAD^+. This follows from their redox potential values, Table III. In contrast, the radicals found from N, NA, i-N, and MN are strong reducing agents and somewhat stronger than the $NAD\cdot$ radical.

(29) P. S. Rao and E. Hayon, *Biochem. Biophys. Res. Commun.*, 51, 468 (1973).

(30) P. S. Rao and E. Hayon, *J. Phys. Chem.*, submitted for publication.

Communications to the Editor

Relative Diylophylic Reactivities of Olefins toward a Trimethylenemethane[1]

Sir:

The cycloadditions of olefins with trimethylenemethane $(1)^2$ or the closely related substance 2-isopropylidenecyclopentane-1,3-diyl $(2)^{3-5}$ are among the

(1) The support of this work by the National Institute of General Medical Sciences (Grant No. GM-16962), the National Science Foundation (Grant No. 33909X), the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Hoffmann-LaRoche Fund is gratefully acknowledged.

(2) For lists of references to early studies in this field see (a) P. Dowd, *Accounts Chem. Res.*, 5, 242 (1972); (b) F. Weiss, *Quart. Rev., Chem. Soc.*, 24, 278 (1970); (c) ref 4.

few examples of intermolecular chemical interception of bidentate diradicals. An accompanying paper[6a] shows that it is possible to observe reactions of both a singlet (S) and a triplet (T) state of the diyl $2.^{6b}$ We report here a quantitative ranking of the rela-

(3) J. A. Berson, R. J. Bushby, J. M. McBride, and M. Tremelling, *J. Amer. Chem. Soc.*, 93, 1544 (1971).

(4) J. A. Berson, D. M. McDaniel, L. R. Corwin, and J. H. Davis, *J. Amer. Chem. Soc.*, 94, 5508 (1972).

(5) J. A. Berson, D. M. McDaniel, and L. R. Corwin, *J. Amer. Chem. Soc.*, 94, 5509 (1972).

(6) (a) J. A. Berson, L. R. Corwin, and J. H. Davis, *ibid.*, 96, 6175 (1974). (b) Although the properties of the singlet permit it to be the bicyclic hydrocarbon 5-isopropylidenebicyclo[2.1.0]pentane, the diyl S provides a simpler formulation at present.
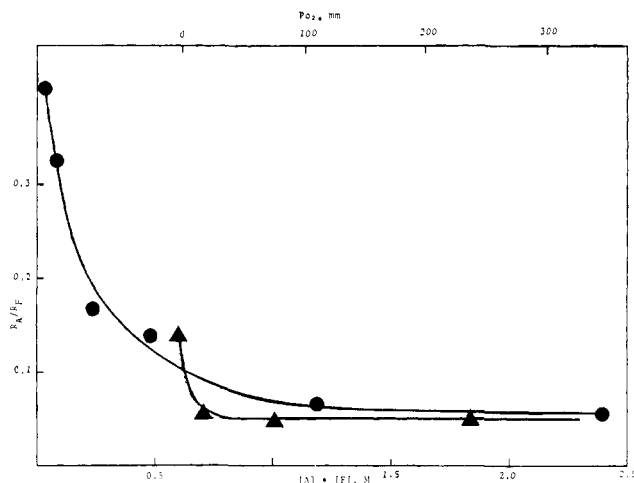
Figure 1. Relative diylophilic reactivity of acrylonitrile (A) vs. dimethyl fumarate (F) as functions of total olefin concentration (circles) and of oxygen pressure admitted to the reaction mixture (triangles).

tive reactivity of a series of nine olefins toward the singlet and of four olefins toward the triplet.

The relative reactivities are determined by observation of the competition between pairs of olefins in forming adducts **4** and **5** from diyl **2**, which is generated in
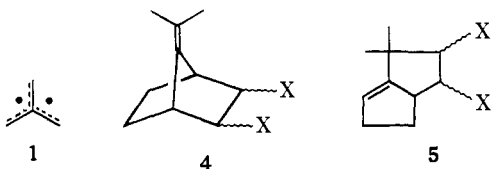
thermal decomposition at 55–65° of azo compound **3** (initial ratio of olefin:azo compound $\sim$8–10, total olefin concentration 1–2 M). The reactions are carried out in carefully degassed acetonitrile solution containing 2-methoxynaphthalene as internal standard. Calibration of the flame ionization detector response for vapor chromatographic (vpc) analysis (10 ft $\times$ $^1/_8$ in. XE-60 or EGP columns) is achieved using known solutions of internal standard and adducts of the bridged series (**4**),[4] prepared by hydrogenation of adducts from the Diels–Alder reaction of the appropriate olefin and 6,6-dimethylfulvene.

The products from the decompositions of the azo compound **3** are shown to be 1:1 adducts of diyl **2** and olefin by vapor chromatography–mass spectrometry. In most cases, the adducts account for >95% of the azo compound decomposed.

A set of gross relative reactivities is derived from the expression $R_i/R_j = (P_i/P_j)(C_j/C_i)$ where R_i/R_j is the reactivity of olefin i relative to that of olefin j toward the diyl **2**, P_i/P_j is the product ratio, and C_j/C_i is the initial olefin ratio. This treatment assumes that the kinetic order in the diyl + olefin reaction is the same for both olefins. The reactivity ratios are spot-checked for internal consistency by matching a given olefin (say i) against two competitors (say j and k) in separate experiments, where it is observed that within experimental error, $(R_i/R_j)(R_j/R_k) = (R_i/R_k)$.

The gross reactivities found at high total olefin concentrations provide, in the case of the more reactive olefins, a good approximate ranking of diylophilicity

toward a thermally generated "parent" diyl. Dilution of the reaction mixtures (while maintaining constant initial ratios of olefins to each other and to azo compound) changes the relative reactivities, as is shown in Figure 1 (circles) for the pair acrylonitrile (A)–dimethyl fumarate (F). Essentially insensitive to total olefin concentration above 1.5 M, the reactivity ratio, R_A/R_F, climbs steeply with further dilution, and, at 0.01 M, it has increased by a factor of 7 over the high-concentration limiting value.

This behavior can be interpreted with Scheme I, in

Scheme I
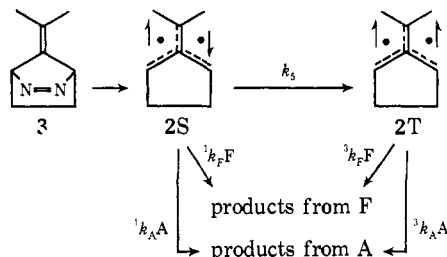
which the "parent" diyl, S, gives rise to at least one additional product-forming "daughter" intermediate, very probably the known[3] triplet diyl, T.

A second set of experiments (Figure 1, triangles) strongly supports this assignment. It shows that (triplet) molecular oxygen restores the high-concentration limiting value of R_A/R_F, even in dilute olefin solutions, undoubtedly by an efficient, selective, irreversible, spin-conserving reaction with T.

From the dilution effect on the product composition it is possible to determine the fraction of the product that is formed from S and that formed from T at any total olefin concentration.[6a] For the weaker diylophiles, the competitively determined gross relative reactivities R_i can be dissected with the aid of two assumptions: that, in the competition experiments, the mixture of cycloadducts formed from a specific olefin is a linear combination of the characteristic product distributions[6a] from the reactions of that olefin with S and with T, and that the intersystem crossing rate for the diyl (k_5 of Scheme I) is independent of the olefin. The observed product distribution from a specific olefin in a competition experiment then can be attributed to fractional S and T contributions, and the ratio of the amounts of singlet products from the two competing olefins, when multiplied by the gross reactivity ratio, R_i/R_j, gives the relative singlet reactivity, $^1k_i/^1k_j$. A similar procedure gives the relative triplet reactivities, $^3k_i/^3k_j$.

The values obtained in this way (Table I) are in good agreement with those determined by other means.[6a] Moreover, Scheme I predicts that the concentration dependence of the gross reactivities should take the form

$$R_A/R_F = [\alpha(\beta C + 1)[F] + \beta\gamma]/[(\beta C + 1)[F] + \gamma]$$

where $\alpha = {}^1k_A/{}^1k_F$, $\beta = {}^3k_A/{}^3k_F$, $\gamma = k_5/{}^1k_F$, and $C = $ [A]/[F]. This equation fits the experimental curve for the degassed runs of Figure 1 within $\pm6\%$ error for each data point with the parameters $\alpha = 0.045$, $\beta = 0.5$, and $\gamma = 0.06$. These values are the same as the defining rate constant ratios (within the estimated uncertainties of the latter) derived from Table I (α and β) and the accompanying paper[6a] (γ).

Table I. Diylophilic Reactivities[a] of Olefins toward Singlet and Triplet States of 2-Isopropylidenecyclopentane-1,3-diyl

Olefin	Rel gross reactivity[b] R	Rel singlet reactivity,[c] $^1R_i = {^1k_i}/{^1k_M}$	Rel triplet reactivity,[c] $^3R_i = {^3k_i}/{^3k_M}$
Maleic anhydride	590	235	
trans-NCCH=CHCN	450	180	
cis-NCCH=CHCN	410	160	
trans-MeO₂CCH=CHCO₂Me	170	67	59
CH₂=C(Me)CN	20		
CH₂=CHCN	10	4	35
CH₂=CHCO₂Me	10	2	11.5
CH₂=C(Me)CO₂Me	7		
cis-MeO₂CCH=CHCO₂Me	(1)	(1)	(1)

[a] In each column, the value for dimethyl maleate (M) is defined as unity. [b] These values are estimated to be accurate to at least ±10%. [c] For experimental errors, see ref 6a.

The reactivities toward the singlet (Table I) roughly parallel the Diels–Alder dienophilic reactivity of these olefins toward cyclopentadiene.[7] Data in the literature[7,8] suggest that for a given group of olefins, the monosubstituted ones lie closer to the high end of the reactivity range in copolymerization reactions than they do in Diels–Alder reactions. The observation (Figure 1, Table I) that the reactivity ratio of acrylonitrile (A) vs. dimethyl fumarate (F) is greater when measured against the triplet than against the singlet [$^3R_A/^3R_F \cong 7(^1R_A/^1R_F)$] therefore is reasonable if the transition states of the triplet and singlet cycloadditions are imagined to resemble those of a free radical addition and a Diels–Alder reaction, respectively.

(7) J. Sauer, H. Wiest, and A. Mielert, Chem. Ber., 97, 3183 (1964).

(8) (a) F. R. Mayo and C. Walling, Chem. Rev., 46, 191 (1950); (b) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, Chapter IV.

(9) National Institute of General Medical Sciences Predoctoral Fellow, 1969–1973 (GM-46,047).

Jerome A. Berson,* Charles D. Duncan, Leonard R. Corwin[9]
Department of Chemistry, Yale University
New Haven, Connecticut 06520

Mechanistic Separation of Singlet and Triplet Reactions of a Trimethylenemethane. Stereospecificity and Regiospecificity in the Cycloadditions of 2-Isopropylidenecyclopentane-1,3-diyl to Olefins[1]

Sir:

Thermal decomposition of the azo compound 1 releases 2-isopropylidenecyclopentane-1,3-diyl, which can be trapped with conjugated olefins, M (XCH=CHX), to give cycloadducts of the fused type F (bicyclo-[3.3.0]octenes), or the bridged type B (7-isopropylidenenorbornenes).[2–4] Supplementing the previous observation[3] that the stereospecificity of formation of cis cycloadducts from cis olefins diminishes as the initial

(2) J. A. Berson, D. M. McDaniel, L. R. Corwin, and J. H. Davis, J. Amer. Chem. Soc., 94, 5508 (1972).

(3) J. A. Berson, D. M. McDaniel, and L. R. Corwin, J. Amer. Chem. Soc., 94, 5509 (1972).

(4) J. A. Berson, C. D. Duncan, and L. R. Corwin, J. Amer. Chem. Soc., 96, 6175 (1974).
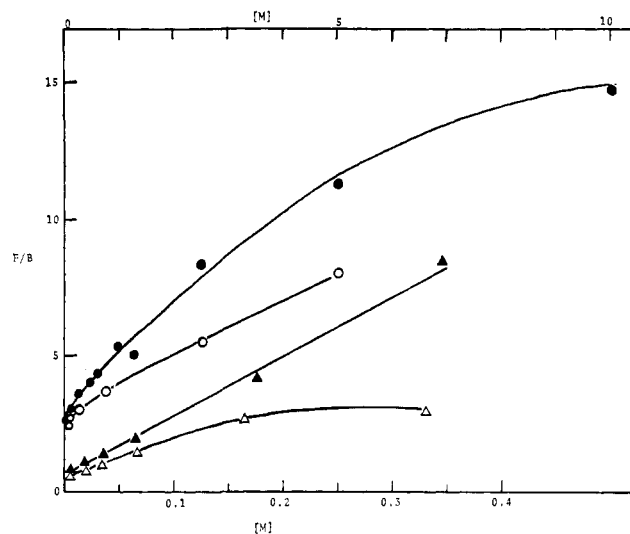
Figure 1. Dependence of the ratio of fused to bridged products (F/B) on the olefin concentration [M]. The upper scale refers to methyl acrylate (O), acrylonitrile (●), and dimethyl maleate (△). The lower scale refers to dimethyl fumarate (▲).

concentration of olefin is decreased, we now find that the regiospecificity also is concentration dependent. A quantitative treatment of these dilution effects provides the basis for a dissection of the reactions of the diyl into those characteristic of two subspecies, a singlet and a triplet (S and T, Scheme I).

Scheme I

X = CO₂Me, CN, etc.
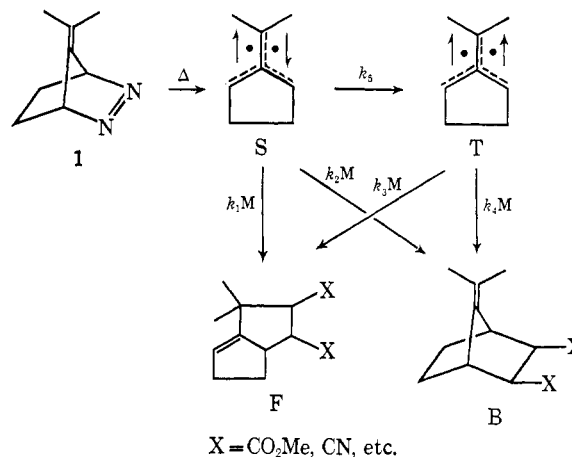
The reaction samples are prepared by dilutions of a stock solution of azo compound 1 and olefin (M) in 1:10 molar ratio in CH₃CN to produce a series in which the initial [M] decreases from 5 to 0.003 M. The solutions are degassed, sealed, pyrolyzed at 60°, and analyzed by gas–liquid chromatography (glc), using 0.125-in. packed or 0.01-in. coated capillary columns in a Perkin-Elmer 900 chromatograph with flame-ionization detector. Figure 1 shows the data on the concentration dependence of the regiospecificity for fused products vs. bridged products (F/B) in reactions of four olefins.

Although the solvent composition is unavoidably inconstant over this range, it is the change in concentration of reactants rather than the change of medium that is responsible for the major effects observed. Independent experiments with a dozen other inert solvents (hydrocarbons, alcohols, halogen compounds) show no sig-